(2) debridement, painful dressing changes and skin grafting, particularly in burn patients. Other situations in which ketamine may be used include diagnostic and operative procedures of the pharynx, larynx, head, eye, ear, nose, anus and mouth (if given with other agents); and certain gynecologic procedures such as dilatation and curettage. Some physicians use ketamine for cardiac catheterization, or when anesthesia must be administered intramuscularly because an intravenous site is not available. It also may be valuable as an induction agent or indicated in poor risk patients or in orthopedic procedures such as closed reductions or manipulations.

The use of ketamine has several drawbacks. One is the apparent ease with which the drug may be administered intravenously or intramuscularly for the production of general anesthesia. This has resulted in administration of ketamine by unqualified persons under adverse circumstances, without adequate knowledge of resuscitation procedures or adequate equipment available. Another drawback is increased intracranial pressure and increased arterial pressure, which may be detrimental to some patients. The drug should be used only by those skilled in respiratory and circulatory support. Another problem with ketamine is the high incidence of untoward reactions on emergence from the drug. These include hallucinations and emergence delirium, including confusion, excitement and irrational behavior. Some patients recall these sensations as extremely unpleasant and request that they never again receive this drug. The frequency with which these emergence reactions occur is said to be approximately 12 percent. Appropriate premedication with a tranquilizer may minimize the frequency of emergence delirium and diminish its magnitude. Careful attention to the circumstances under which the patient awakens, including minimal stimulation, is believed also to diminish the frequency and severity of emergence complications, but it may be dangerous for patients to be allowed to recover in darkened seclusion.

Recently the use of low-dose ketamine (that is ¼ to ½ mg per kg of body weight given intravenously, compared with 2 mg or more per kg of body weight given intravenously) has become of great interest. The available evidence suggests that emergence delirium is absent with low-dose techniques. However, additional studies are needed before this claim can be accepted with certainty.

In summary, ketamine is a valuable drug that is neither as good as enthusiasts nor as bad as its detractors claim. Each anesthesiologist must work with ketamine and after appropriate experience decide what role it will have in his practice.

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**REFERENCE**

Wilson RD: Current status of ketamine, chap 12, *In* Hershey SG (Ed): The American Society of Anesthesiologists Regional Refresher Courses in Anesthesiology. Highland Park, Ill. Lippincott Co., Vol 1. 1973, pp 157-167

## Present Status of Muscle Relaxants and Antagonists

MODERN SURGERY has benefited significantly from the introduction of neuromuscular blocking agents. Curare (d-turbocurarine) has been used clinically since the 1940's with generally satisfying results. While maintenance of skeletal muscle relaxation during surgical operation in most instances has been carried out successfully with this agent, for endotracheal intubation and for shorter surgical procedures a muscle relaxant with rapid onset and short duration of action is required. Succinylcholine, a synthetic agent introduced in 1951, fulfilled some of the requirements and was widely used. Significant side effects, however, may occur with each of these agents.

The shortcomings of d-tubocurarine are: (a) hypotension due to ganglionic blockade and occasional histamine release with associated skin reactions or rarely bronchial spasm, or both, and (b) relatively slow onset and long duration of action—the latter necessitating the frequent use of reversing agents of the anticholinesterase type (such as neostigmine and pyridostigmine). Clinical problems with succinylcholine are entirely different. This agent is not amenable to pharmacological reversal and its depolarizing action on the motor end-plate produces muscle fasciculations and muscle pains. Its duration of action depends on the rate of inactivation by plasma cholinesterase. Deficiency or abnormality of this enzyme and accidental overdose of the agent may produce extremely long lasting paralysis for which artificial ventilation is the only effective measure. Increased intraocular pressure, dysrythmias, cardiac conduction abnormalities due to potassium release, postoperative myalgia and possibly very injurious hyperthermia are additional drawbacks to the use of succinylcholine. For these reasons research continued for new and superior muscle relaxant agents.

In the United States, gallamine, a curare-like

compound with shorter duration of action, and pancuronium, with fewer side effects than tubocurarine, were introduced. Gallamine, and to a lesser extent, pancuronium, produce tachycardia. Pancuronium, because of its lack of hypotensive action currently is gaining wide acceptance. Dimethyl tubocurarine, a long known but clinically neglected agent, seems to be reentering clinical practice because of its minimal circulatory effects.

The present consensus favors introduction of a curare type nondepolarizing muscle relaxant with shorter onset and duration of action than presently available. Some compounds of this type were developed in recent years, but most of them fell short of clinical requirements. As a consequence, the reversal of the existing, longer-acting agents remains a problem of patient management.

A further variant of drug application in this field is the substitution of glycopyrrolate in place of atropine in the "reversing process." Less tachycardia and dysrhythmias are claimed with this agent during the reversing process.

Development of new rapidly acting, evanescent neuromuscular blocking agents whose intensity of action can be regulated by continuous adjustment of the rate of administration, and improvements on the techniques of pharmacological reversal of the existing agents are two realistic avenues through which optimal therapeutic conditions in this clinical field may be achieved.

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**REFERENCES**

Katz RL: Pyridostigmine (Mestinon®) as an antagonist of d-tubocurarine. Anesthesiology 28:528-534, May-Jun 1967

Ramamurthy S, Shaker MH, Winnie AP: Glycopyrrolate as a substitute for atropine in neostigmine reversal of muscle relaxant drugs. Can Anaesth Soc J 19:399-411, Jul 1972

Savarese JJ, Kitz RJ: Does clinical anesthesia need new neuromuscular blocking agents? Anesthesiology 42:236-239, Mar 1975

Gyermek L: Clinical studies on the reversal of the neuro-muscular blockade produced by pancuronium bromide—I. The effect of glycopyrrolate and pyridostigmine. Curr Ther Res 18:377-382, Sep 1975

## Chronic Pain Management: Developing Trends

CHRONIC benign and functional pain syndromes are yielding to pharmacologic and psychologic study to show a surprising variety of diagnostically distinct and therapeutically manageable entities.

Spinal anesthesia was applied systematically in these syndromes in the 1930's. However, this was not widely exploited until this decade as the differential spinal block. This technique utilizes intrathecal injections of solutions at ten-minute intervals beginning with a 0.9 percent solution of sodium chloride. This is followed by procaine solutions in increasing concentrations of 0.25 percent, 0.5 percent, 1 percent and 2 percent. The saline solution is a placebo and the procaine solutions sequentially block the sympathetic, somatic and motor divisions of the central nervous system. Pain which is relieved by placebo or is not relieved by paretic or paralytic concentrations is interpreted as central pain and can be further evaluated with psychologic testing. Central pain syndrome implies that the pain complaint is resistant to peripheral somatic interventions and is independent of peripheral pathology, such as laminectomy scars. Relief by placebo implies cortical control over the pain complaint.

Using this technique, Winnie reported on a series of patients with bizarre back and leg pains which were relieved by sympatholytic concentrations of procaine. This suggests either vascular problems or occult sympathalgias (reflex sympathetic dystrophies) in 75 percent of patients with pain of unknown cause. Relief by somatic block suggests an organic basis for pain. However, painful muscle spasm secondary to anxiety is relieved by somatic block although it is a reflection of a psychologic state. Differential block has resulted in a change in diagnosis in 59 percent of patients seen at the Stanford Medical Center's Pain Clinic. When the Minnesota Multiphasic Personality Inventory (MMPI) is used to evaluate central pain states further, characteristically the pain complaint represents depression, anxiety or hysteria. In patients for whom findings on psychological tests are normal, pain may be related to persistent environmental reinforcement (operant conditioning), for example, in seeking affection from an inattentive spouse. Another group in this category is existential pain in which the pain gives meaning to life often in a religious or social context. Central pain may also result from anatomic neural damage, such as tabes dorsalis or thalamic syndrome.

Phenothiazines and the tricyclic antidepressants are remarkably effective in the management of pain as a manifestation of anxiety-depression. Supportive psychotherapy is useful for hysterics, and behavior modification is helpful for patients with the "habit" of a pain complaint. In patients for whom the cause of the pain syndrome is refractory to specific treatment or is still uncertain, development of coping skills is of benefit. This